

AMENDMENTS TO THE CLAIMS

1. **(Currently amended)** A recombinant nucleotide sequence which codes upon expression for at least a part of a bifunctional hybrid active-site serine β -lactamase protein, wherein the β -lactamase protein is bearing at least one heterologous sequence, ~~characterized in that wherein the β -lactamase hybrid protein is bearing the heterologous sequence in a region located between two neighboring alpha helices of the β -lactamase sequence, wherein the region is forming a juncture between the alpha helices of active-site serine β -lactamases, wherein said alpha helices correspond to the last two alpha helices before the alpha/beta domain, and wherein the hybrid protein is~~ having two functions, the first function is associated with the β -lactamase portion and the second function is associated with the heterologous sequence having a biological function which is different from the first function.

2. **(Canceled)**

3. **(Canceled)**

4. **(Currently amended)** The recombinant nucleotide sequence according to ~~any of~~ claims Claim 1 to 3, ~~characterized in that wherein~~ the β -lactamase protein is bearing at least one heterologous sequence in a region located between two neighboring alpha helices of the β -lactamase sequence, wherein the region is selected from:

a) the region forming a juncture between alpha helix 8 and alpha helix 9 of TEM-1 β -lactamase;

b) the region forming a juncture between the alpha helices which are homologous to alpha helix 8 and alpha helix 9 of TEM-1 β -lactamase.

5. **(Currently amended)** The recombinant nucleotide sequence according to ~~any of~~ claims Claim 1 to 4, ~~characterized in that wherein~~ the β -lactamase moiety is selected from the group:

a) class A β -lactamase,

b) class C β -lactamase,

c) class D β -lactamase,

d) a recombinant sequence of one or more of a) to c).

6. **(Currently amended)** The recombinant nucleotide sequence according to ~~any of~~ claims 1 to 5, ~~characterized in that wherein~~ the β -lactamase moiety is derived from class A β -

lactamase, wherein β -lactamase class A protein is bearing the heterologous sequence in the region forming a juncture between alpha helix 8 and alpha helix 9:

7. **(Currently amended)** The recombinant nucleotide sequence according to claim 6, ~~characterized in that~~ wherein the region forming a juncture between alpha helix 8 and alpha helix 9 is selected from the group:

- a) the amino acid sequence Thr195 to Leu199 of the TEM-1 β -lactamase;
- b) the amino acid sequence corresponding to the amino acid sequence Thr195 to Leu199 in TEM-1 β -lactamase.

8. **(Currently amended)** The recombinant nucleotide sequence according to ~~any of~~ claims Claim 1 to 5, ~~characterized in that~~ wherein the β -lactamase moiety is derived from class C β -lactamase, wherein β -lactamase class C protein is bearing the heterologous sequence in the region forming a juncture between alpha helices, which correspond to alpha helix 8 and alpha helix 9 in TEM-1 β -lactamase.

9. **(Currently amended)** The recombinant nucleotide sequence according to claim 8, ~~characterized in that~~ wherein the region forming a juncture is selected from the group:

- a) the amino acid sequence K239 to E245 of the AmpC β -lactamase;
- b) the amino acid sequence corresponding to the amino acid sequence K239 to E245 of the AmpC β -lactamase.

10. **(Currently amended)** The recombinant nucleotide sequence according to ~~any of~~ claims Claim 1 to 5, ~~characterized in that~~ wherein the β -lactamase moiety is derived from class D β -lactamase, wherein β -lactamase class D protein is bearing the heterologous sequence in the region forming a juncture between alpha helices, which correspond to alpha helix 8 and alpha helix 9 in TEM-1 β -lactamase.

11. **(Currently amended)** The recombinant nucleotide sequence according to claim 10, ~~characterized in that~~ wherein the region forming a juncture is selected from the group:

- a) the amino acid sequence N510 to F514 of the BlaR-CTD β -lactamase;
- b) the amino acid sequence corresponding to the amino acid sequence N510 to F514 of the BlaR-CTD β -lactamase.

12. **(Currently amended)** A recombinant nucleotide sequence which codes upon expression for at least a part of a bifunctional hybrid β -lactamase class A protein, ~~characterized~~

Int. Appl. No. : PCT/EP2005/050174
Int. Filing Date : January 17, 2005

~~in that~~ wherein the β -lactamase class A protein is bearing at least one heterologous sequence in a region located between two neighboring alpha helices of the β -lactamase sequence, wherein the region is selected from:

a) the region forming a juncture between alpha helix 8 and alpha helix 9 of the TEM-1 β -lactamase;

b) the region forming a juncture between the alpha helices of homologous β -lactamases class A, said alpha helices corresponding to the alpha helix 8 and alpha helix 9 of the TEM-1 β -lactamase, and

wherein the hybrid protein is having two functions, the first function is associated with the β -lactamase portion and is selected from

c) hydrolyzing β -lactams (β -lactamase activity);

d) binding covalently and in a stable manner to substances selected from the group β -lactams, derivatives of β -lactams, inhibitors of β -lactams;

wherein the second function is associated with the heterologous sequence having a biological function which is different from the first function.

13. (Canceled)

14. (Canceled)

15. (Currently amended) The recombinant nucleotide sequence according to ~~any one of claims~~ Claim 1 to 14, wherein the three-dimensional structure of the β -lactamase portion of the hybrid β -lactamase is homologous to the three-dimensional structure of the TEM-1 β -lactamase.

16. (Currently amended) The recombinant nucleotide sequence according to ~~any one of claims~~ Claim 1 to 15, wherein the heterologous sequence has a length of 11 or more amino acid residues.

17. (Currently amended) The recombinant nucleotide sequence according to ~~any one of claims~~ Claim 1 to 15, wherein the heterologous sequence has a length of 18 or more amino acid residues.

18. (Currently amended) The recombinant nucleotide sequence according to ~~any one of claims~~ Claim 1 to 15, wherein the heterologous sequence has a length of 25 or more amino acid residues.

19. **(Currently amended)** The recombinant nucleotide sequence according to ~~any one~~ of claims Claim 1 to ~~15~~, wherein the heterologous sequence has a length of 50 or more amino acid residues.

20. **(Currently amended)** The recombinant nucleotide sequence according to ~~any one~~ of claims Claim 1 to ~~15~~, wherein the heterologous sequence has a length of 100 or more amino acid residues.

21. **(Currently amended)** The recombinant nucleotide sequence according to ~~any one~~ of claims Claim 1 to ~~20~~, wherein the nucleotide sequence coding for the β -lactamase sequence is selected from:

- a) nucleotide sequence coding for the β -lactamase TEM-1 (SEQ ID NO: 1)
- b) nucleotide sequence coding for the β -lactamase BlaP (SEQ ID NO: 2);
- c) nucleotide sequence coding for the β -lactamase BlaL (SEQ ID NO: 3);
- d) nucleotide sequence coding for the β -lactamase AmpC (SEQ ID NO: 39);
- e) nucleotide sequence coding for the β -lactamase BlaR-CTD (SEQ ID NO: 41);
- f) a recombinant sequence of one or more of a) to e);
- g) nucleotide sequences which hybridise under stringent conditions to the nucleotide sequences of any one of a) to f) or fragments thereof.

22. **(Currently amended)** The recombinant nucleotide sequence according to ~~any one~~ of claims Claim 1 to ~~21~~, wherein the heterologous sequence is related to a function selected from: being an epitope, being a specific binding partner for antibodies, being specifically recognized and bound by antibodies, having a binding affinity to earth alkali and metal ions, having enzymatic activity, being a toxin (STa heat-stable enterotoxin of *E. coli*), bearing a glycosylation site, bearing a glycosylated peptide, being a specific binding partner for any polypeptide or any ligand, having a binding affinity to dsDNA and ssDNA or RNA (having a binding affinity to nucleotide and polynucleotide).

23. **(Currently amended)** The recombinant nucleotide sequence according to ~~any one~~ of claims Claim 1 to ~~22~~, wherein the heterologous sequence is selected from the group: STa (heat stable enterotoxin of *Escherichia coli*, SEQ ID NO: 21), protein A of *Staphylococcus aureus*, (SEQ ID NO: 23 and 25), protein G of *Streptococcus pyogenes*, (SEQ ID NO: 27 and 29), a linear antigenic determinant of the hemagglutinin of the ~~Influenza~~ Influenza virus (SEQ ID NO:

Int. Appl. No. : **PCT/EP2005/050174**
Int. Filing Date : **January 17, 2005**

31), a fragment of human phospholipase-type 11 (hPLA2) (SEQ ID NO: 33), LPS binding amino acid sequence (SEQ ID NO: 35), and nucleotide sequences which hybridise under stringent conditions to said nucleotide sequences or fragments thereof.

24. **(Canceled)**

25. **(Currently amended)** A recombinant polypeptide comprising at least a part of a bifunctional hybrid active-site serine β -lactamase protein, wherein the β -lactamase protein is bearing at least one heterologous sequence, wherein the β -lactamase protein is bearing at least one heterologous sequence in a region located between two neighboring alpha helices of the β -lactamase sequence, wherein the region is forming a juncture between the alpha helices of active-site serine β -lactamase, wherein said alpha helices correspond to the last two alpha helices before the alpha/beta domain, and ~~characterized in that~~ wherein the hybrid protein is having two functions, the first function is associated with the β -lactamase portion and the second function is associated with the heterologous sequence having a biological function which is different from the first function.

26.-53. **(Canceled)**